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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/280,020	03/29/99	DUPBE J	241/145

HM22/0618

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EXAMINER	
NOLAN, P	
ART UNIT	**PAPER NUMBER**
1644	4

DATE MAILED: 06/18/99

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

PTO-90C (Rev. 2/95)

1- File Copy

Office Action Summary

Application No.	Applicant(s)
09/280,020	Dupre
Examiner	**Group Art Unit**
Nolan	1644

—The MAILING DATE of this communication appears on the cover sheet beneath the correspondence address—

Period for Response

A SHORTENED STATUTORY PERIOD FOR RESPONSE IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a response be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for response specified above is less than thirty (30) days, a response within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for response is specified above, such period shall, by default, expire SIX (6) MONTHS from the mailing date of this communication .
- Failure to respond within the set or extended period for response will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).

Status

☒ Responsive to communication(s) filed on 3-29-99.

☐ This action is **FINAL.**

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle,* 1935 C.D. 1 1; 453 O.G. 213.

Disposition of Claims

☒ Claim(s) 15-34 is/are pending in the application.

Of the above claim(s) _____ is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) 15-34 is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claim(s) _____ are subject to restriction or election requirement.

Application Papers

☒ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119 (a)-(d)

☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 11 9(a)-(d).

☒ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☒ received in Application No. (Series Code/Serial Number) 08/737,446.

☐ received in this national stage application from the International Bureau (PCT Rule 1 7.2(a)).

*Certified copies not received: _____.

Attachment(s)

☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____

☒ Notice of References Cited, PTO-892

☒ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Interview Summary, PTO-413

☐ Notice of Informal Patent Application, PTO-152

☐ Other _____

Office Action Summary

Part III DETAILED ACTION

1. Claims 15-34 are pending.

2. This application does not contain an abstract of the disclosure as required by 37 CFR 1.72(b). An abstract on a separate sheet is required.

3. Claims 18, 23, 28 and 33 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicant has no specific support for the species GLP 1 (7-36), in their specification or claims as originally filed. It is suggested Applicant amend their claims to GLP 1 (7-37).

4. Claims 15-18, 20-23, 25-28 and 30-33 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the use of GLP 1 (7-36) amide or GLP 1 (7-37) in treating Type I diabetes, does not reasonably provide enablement for the use of any analog to GLP 1 (7-36) amide. The specification does not enable any person skilled in the art to which it pertains, or with which it is most clearly connected, to use the invention commensurate in scope with these claims.

Claims 15-18, 20-23, 25-28 and 30-33 recite the use of an analogue to GLP 1 (7-36) amide or GLP 1 (7-36) to treat Type I diabetes, however, the present specification fails to disclose any other peptide which has GLP 1 (7-36) amide or GLP 1 (7-37) activity in treating diabetes. In addition, the specification provides no guidance as to which of the 30 amino acids may be changed while GLP 1 (7-36) amide activity is retained. The total number of 30 amino acid peptides is 3.4×10^{29}. The number of single amino acid substitutions is 600. Because of this lack of guidance, the extended experimentation that would be required to determine which substitutions would be acceptable to retain GLP 1 (7-36) amide or GLP 1 (7-37) activity, and the fact that the relationship between the sequence of a peptide and its tertiary structure (i.e. its activity) are not well understood and are not predictable (e.g. see Ngo et al., (W), newly cited, in The Protein Folding Problem and Tertiary Structure Prediction,1994, Merz et al., (ed.), Birkhauser, Boston, MA, pp. 433 and 492-495.), it would require an undue amount of experimentation for one of skill in the art to arrive at the other 3.4×10^{29} peptides that have GLP 1 (7-36)amide or GLP 1 (7-37) activity.

Double Patenting

The non-statutory double patenting rejection, whether of the

obviousness-type or non-obviousness-type, is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent. *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969); *In re Vogel,* 422 F.2d 438, 164 USPQ 619 (CCPA 1970); *In re Van Ornum,* 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Longi,* 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); and *In re Goodman,* 29 USPQ2d 2010 (Fed. Cir. 1993).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(b) and (c) may be used to overcome an actual or provisional rejection based on a non-statutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.78(d). Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

5. Claims 15-34 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 38-47 of copending Application No. 08/737,446 in view of WO 93/18786 (N).

Claims 38-47 in copending Application No. 08/737,446 recite a method of treating Type I diabetes mellitus comprising administering GLP-1 or an agonist thereof in claims 43-47 and co-administration of insulin and GLP-1 or agonist thereof in claims 38-42, subcutaneously.

The claimed invention in the instant application differs from the claimed invention in copending Application No. 08/737,446 by the recitation of administering the GLP-1 amide or analog thereof nasally or orally with coadministration of insulin.

However, the `786 patent teaches that nasal administration of GLP-1 is particularly advantageous from a patient compliance point of view and that GLP-1 oral administration is preferred in instances where extent and kinetics of absorption is not a critical issue (page 8-9, in particular).

One of ordinary skill in the art at the time the invention was made would have been motivated to treat Type I diabetics with GLP-1(7-36)amide and insulin by an oral or nasal route because the '786 patent teaches that nasal administration of GLP-1 is particularly advantageous from a patient compliance point of view and that GLP-1 oral administration is preferred in instances where extent and kinetics of absorption is not a critical issue. From the recitations in claims 15-34 of copending Application No. 08/737,446 and the teachings of the '786 patent, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole is prima facie obvious to one of ordinary

skill in the art at the time the invention was made.

This is a provisional obviousness-type double patenting rejection.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. § 103 which forms the basis for all obviousness rejections set forth in this Office action:

A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Subject matter developed by another person, which qualifies as prior art only under subsection (f) or (g) of section 102 of this title, shall not preclude patentability under this section where the subject matter and the claimed invention were, at the time the invention was made, owned by the same person or subject to an obligation of assignment to the same person.

6. Claims 15-17, 19-22, 24-27, 29-32 and 34 are rejected under 35 U.S.C. § 103 as being unpatentable over Gutniak et al. (U), in view of U.S. Patent 5,424,286, (A), D'Alessio et al., (V), and WO 93/18786 (N).

Gutniak et al., teaches the intravenous use of GLP 1(7-36)amide (i.e. GLP-1 or GLIP) in Type I diabetes, wherein GLP 1(7-36)amide decreased the need for insulin dosage required to maintain euglycemia (see abstract, in particular). Gutniak et al., also teaches that GLP-1(7-36)amide exerted strong insulinotropic effects in vitro and in vivo (see page 1316, in particular). Lastly Gutniak et al., teaches co-administration of insulin with GLP-1 in type I diabetics prior to the feeding of a meal, wherein the addition of GLP-1 to the treatment regimen significantly decreased the need for insulin to maintain euglycemia (see page, 1317).

The claimed invention differs from the prior art teachings only by the recitation of treating Type I diabetics with GLP-1(7-36)amide or an analogue thereof orally or nasally. However, in summarizing the use of the Gutniak et al., findings, the `286 patent teaches that "In patients with IDDM (i.e. Type I diabetes), the GLIP (i.e. GLP-1(7-36)amide) treatment lowered the insulin required by one half. This glucose dependent activity is a very desirable characteristic for a therapeutic agent that can be used to treat DM avoiding the complications of hypoglycemic side effects" (column 1, in particular). In addition, D'Alessio et al., also summarized to findings of Gutniak et al., by stating "It has recently been reported that infusions of GLP-1 into diabetic

subjects decreased the insulin dosage required to maintain euglycemia. Furthermore, type I diabetic subjects treated with GLP-1 during one step euglycemic, hyperinsulinemic clamps had 10-15% higher rates of glucose than during control studies, thereby suggesting that GLP-1 may promote glucose uptake in addition to augmenting insulin release" (page 2263, 2nd column, in particular). Lastly, the `786 patent teaches that nasal application of GLP-1 is particularly advantageous from a patient compliance point of view and that GLP-1 oral administration is preferred in instances where extent and kinetics of absorption is not a critical issue (page 8-9, in particular).

One of ordinary skill in the art at the time the invention was made would have been motivated to treat Type I diabetics with GLP-1(7-36)amide and insulin because GLP-1 decreased the need for insulin co-administration to maintain euglycemia as taught by Gutniak et al., and the glucose dependent activity of GLP-1 is a very desirable characteristic for a therapeutic agent that can be used to treat diabetes mellitus avoiding the complications of hypoglycemic side effects, as taught by the '286 patent and administer GLP-1 by an oral or nasal route since the `786 patent teaches that nasal application of GLP-1 is particularly advantageous from a patient compliance point of view and that GLP-1 oral administration is preferred in instances where extent and kinetics of absorption is not a critical issue . The results of the Gutniak et al., teachings, when viewed from the point of view of those skilled in the art (i.e. the '286 patent and D'Alessio et al.) would reasonably motivate one of skill in the art to treat Type I diabetics with GLP-1(7-36)amide and insulin with a reasonable expectation of success. From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole is prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references.

7. The lengthy specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicants cooperation is requested in correcting any errors of which applicant may become aware of in the specification.

8. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Patrick Nolan whose telephone number is (703) 305-1987. The examiner can normally be reached on Monday through Friday from 8:30 am to 4:30 pm.

9. If attempts to reach the examiner are unsuccessful, the examiner's supervisor, Christina Chan, can be reached at (703) 305-3973. The FAX number for our group, 1644, is (703) 305-7401. Any

inquiry of a general nature relating to the status of this application or proceeding should be directed to the Group receptionist, whose telephone number is (703) 308-0196

Patrick J. Nolan, Ph.D.
June 15, 1999

Patrick J. Nolan, Ph.D.
Patent Examiner
Group 1640